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EXAMINER

BHAT, NARAYAN KAMESHWAR

ART UNIT

PAPER NUMBER

1634

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/501,162	BOSNES, MARIE	
	<b>Examiner</b>	<b>Art Unit</b>	
	NARAYAN K. BHAT	1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 October 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-25 and 34-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 and 34-36 is/are rejected.
- 7) ☒ Claim(s) 1-4, 13, 15, 21-24 and 34-36 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/12/2011</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **FINAL ACTION**

1. This office action is written in response to the papers filed on October 27, 2010. Applicant has amended claims 1-16, 18 and 21-25 and added new claims 34-36. The claim amendments requiring numerous new limitations necessitated the new grounds of rejection presented in this office action. Accordingly, ***this action is made final.***

### ***Claim Status***

2. Claims 1-25 and 34-36 are pending in this application. Claims 1-16, 18 and 21-25 are amended and new claims 34-36 are added. Claim amendments have been reviewed and entered.

The previous rejection of claims 1, 3, 5-12, 15-20, 24 and 25 under 35 USC 103 (a) as being obvious over Schubler in view of Lubenow et al in the office action dated April 27, 2010 has been withdrawn in view of claim amendments and persuasive arguments made by the Applicant. The previous rejection of claims 1, 2 and 22 under 35 USC 103 (a) as being obvious over Schubler in view of Lubenow et al and further in view of Ekenberg et al in the office action dated April 27, 2010 has been withdrawn in view of claim amendments and persuasive arguments made by the Applicant. The previous rejection of claims 1, 3-4, 13-14, 21 and 23 under 35 USC 103 (a) as being obvious over Schubler in view of Lubenow et al and further in view of Safarik et al in the office action dated April 27, 2010 has been withdrawn in view of claim amendments and persuasive arguments made by the Applicant. Applicant's arguments filed on October 27, 2010 have been fully considered and addressed following the claim rejections.

3. Claims 1-25 and 34-36 are under prosecution.

### ***Claim Objections***

4. Claims 1-4, 13, 15, 18, 21-24 and 34-36 are objected to because of the following informalities. Claims 1-4, 13, 15, 21-24 and 34-36 recite the phrase “first particulate solid supports.” It appears that the term “magnetic” is missing between the “first” and “particulate.” Applicant is suggested to use the phrase “first magnetic particulate solid supports” for the clarity and maintaining the consistency of the previous recitation of the phrase “first magnetic particulate solid supports” throughout the claim recitation. Appropriate correction is required.

Claims 1, 3 and 13 are also objected to because of the following informalities. Claims 1, 3 and 13 recite the phrase “second particulate solid supports.” It appears that the term “magnetic” is missing between the “second” and “particulate.” Applicant is suggested to use the phrase “second magnetic particulate solid supports” for the clarity and maintaining the consistency of the previous recitation of the phrase “second magnetic particulate solid supports” throughout the claim recitation. Appropriate correction is required.

### ***Specification***

5. The amendment filed on October 27, 2010 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added

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material which is not supported by the original disclosure is as follows: “a plurality of first magnetic particulate solid supports”, “a plurality of second magnetic particulate solid supports” and “a plurality of third particulate solid supports” (the new matter phrases are underlined by the Examiner).

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections - 35 USC § 112-First paragraph***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***New Matter Rejection***

7. Claims 1-25 and 34-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes, “If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph written description requirement (In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).”

In the instant case, the following imitations represent new matter: “a plurality of first magnetic particulate solid supports”, “a plurality of second magnetic particulate solid supports” and “a plurality of third particulate solid supports” in claims listed above in

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section 3 and separating the plurality of first particulate solid supports to which are bound nucleic acid components and the second plurality of particulate solid supports to which are bound protein components from unbound components in the sample in instant claim 1 (the new matter phrases are underlined by the Examiner).

Applicant has cited support for claims 1-16, 18, 21-25 and 34-36 throughout the specification, for example, at page 34, lines 13-23; page 36, lines 19-32; page 39, lines 17-23; page 40, line 15 through page 43, line 5 and FIG. 7. Although cited support in the specification refers to the "second solid support" or "a plurality of solid supports" in general terms, no specific basis for the plurality of the first or the second magnetic particulate solid supports or the third particulate solid supports and separating from unbound sample is identified. Furthermore, reviews of the specification by the examiner find any basis for the new limitations as discussed above.

Furthermore, "the written description requirement prevents an applicant from claiming subject matter that was not adequately described in the specification as filed. New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads)." (MPEP § 2163).

Since Applicant has not identified specific citations of support in the instant specification as originally filed or in the original claims for the above underlined limitations, Applicant is required to cancel the new matter in the reply to this Office Action or identify the new matter in the specification as originally filed.

### ***Claim Interpretation***

8. Instant claim 1 recite “a plurality of first magnetic particulate solid supports” and “a plurality of second magnetic particulate solid supports.” The instant specification does not provide a limiting definition for “a plurality of first or second magnetic particulate solid supports.” Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding the first and the second magnetic particulate solid supports (In re Hyatt, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). Given the broadest reasonable interpretation the “a plurality of the first and the second magnetic particulate solid supports” are interpreted broadly as magnetic solid supports for the nucleic acid isolation or the protein isolation respectively. The third particulate solid supports or a plurality of solid particles are interpreted broadly to encompass either magnetic or non-magnetic particles.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1-25 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kleiber et al (USPN 6,255,477 issued Jul. 3, 2001) in view of Lubenow et al (USPN 6,723,510 issued Apr. 20, 2004) and further in view of Schubler et al (TIG, 1995, 11, 378-379). The negative surface charge of Si-OH group of Kleiber et al as used for the rejection of claim 34 is further evidenced by Behrens et al (Journal of Chemical Physics, 2001, 115, 6716-6721).

Claim 1 is drawn to isolating a nucleic acid and a protein from each other in a sample using magnetic particles capable of binding to either the nucleic acid or the protein. As discussed below Kleiber et al teaches a method of isolating the nucleic acids with the magnetic particles with glass surface binding to the nucleic acids in a sequence independent manner and Lubenow et al teaches magnetic particles with ion exchange resins for isolating proteins by effecting chromatographic interactions. Schubler et al teaches a method for isolating the nucleic acids and proteins from the same sample.

Regarding claim 1, Kleiber et al teaches a method of isolating the nucleic acids and proteins from each other in a sample and the method comprising providing a sample that compresses nucleic acid components and protein components (e.g., bacterial or animal cells; column 5, lines 9-22 and column 6, lines 4-10) and further teaches contacting the sample with a plurality of magnetic particles (i.e., magnetic particulate solid supports) comprising glass surface binding to the nucleic acid components in the sample (Fig. 1 and column 5, lines 35-42 and column 8, lines 8-56).

Kleiber et al also teaches that the magnetic solid support comprises a hydroxyl group on the glass surface (i.e., Si-OH; column 3, lines 14-57) and binds to a plurality of DNA in a sample (e.g., Fig. 4 and Example 4), thus teaching the magnetic particles with glass surface binds to the DNA in a sequence independent manner. It is also noted that the magnetic solid supports (i.e., particles) comprising the hydroxyl groups are the preferred solid supports for binding the nucleic acids in a sequence independent manner as recited in the instant specification (USPGPUB, paragraph 0152).

Kleiber et al further teaches that the magnetic particles (i.e., magnetic particulate solid supports) coated with streptavidin are used for isolating the proteins (column 2, lines 1-6). The combined teachings of a plurality of magnetic particles with glass surface and a plurality of magnetic particles coated with streptavidin of Kleiber et al encompasses the first magnetic particulate solid supports and the second magnetic particulate solid supports. Kleiber et al do not teach explicitly the binding of proteins to the second magnetic particulate solid supports by effecting a chromatographic interactions and separating the plurality of first magnetic particulate solid supports and the second magnetic particulate solid supports bound to the proteins from unbound components in the sample.

However magnetic particles for protein isolation by effecting chromatographic interactions were known in the art at the time the claimed invention was made as taught by Lubenow et al.

Lubenow et al teaches method for separation and isolation of nucleic acids and proteins from a sample using magnetic particles (column 3, lines 45-67) and further

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teaches oligodT magnetic particles for binding polyA RNA (i.e., nucleic acids; column 5, lines 38-67 and column 6, lines 1-27). Lubenow et al also teaches the magnetic particles comprising ion exchange resins, hydrophobic interactions resins or nickel-nitrilotriacetic acids (Example 1 and column 2, lines 15-37 and column 10, lines 15-42), which are involved in chromatographic interactions as recited in the instant specification (USPGPUB, paragraph 0056). Lubenow et al also teaches distinct supports for binding proteins and RNA (column 5, lines 40-59), thus teaching the first magnetic particulate solid supports and the second magnetic particulate solid supports.

The combined teachings of Kleiber et al and Lubenow et al provide solid supports to which nucleic acids components binds are distinct from solid supports to which proteins bind. The magnetic particles of Lubenow et al for protein isolation are deemed to work in the combined isolation of nucleic acids and proteins in the method of Kleiber et al because the sample and the buffer used for the nucleic acids and protein isolation are the same in the method of Kleiber et al (column 5, lines 54-60) and Lubenow et al (column 4, lines 13-27).

Lubenow et al also teaches magnetic particles comprising ion exchange interactions improves the yield of protein molecules of interest, reproducibility of the isolation method (column 5, lines 7-22).

It would have been prima facie obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the protein isolation method of Kleiber et al with the magnetic solid supports comprising ion exchange interactions of Lubenow et al with a reasonable expectation of success.

An artisan would have been motivated to modify the protein isolation method of Kleiber et al with the expected benefit of having magnetic particles for protein isolation for improving the yield of protein molecules of interest and reproducibility of the protein isolation method and increasing the signal to noise ratios of protein molecules of interest as taught by Lubenow et al (column 5, lines 7-22). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves substituting streptavidin magnetic particles with magnetic particles with ion exchange interactions.

Both Kleiber et al and Lubenow et al do not teach explicitly using the same sample for the nucleic acid and the protein isolation. However, the use of the same sample for both the nucleic acid and protein isolation was known in the art at the time the claimed invention was made as taught by Schubler et al.

Schubler et al teaches a combined isolation of nucleic acids and proteins from a sample using oligo dT magnetic beads for isolating polyA RNA and using the supernatant from the same sample for isolating the DNA and the proteins (Figs. 1 and 2 and pg. 378, paragraphs 2 and 3, pg. 379, paragraphs 1 and 2), thus teaching separating the nucleic acids (i.e., the poly A RNA) bound to the magnetic beads and isolating the proteins from the unbound components in the sample. Schubler et al further teaches the combined isolation of nucleic acids and proteins allows to use the small amounts of the sample for genetic and protein analysis (Figs. 1 and 2 and pg. 378, first paragraph and pg. 379, last paragraph) for correlating the genotypic and phenotypic relationship.

As described above, both Kleiber et al and Lubenow et al teaches a method for isolating DNA and proteins from a sample using magnetic solid supports and Schubler et al merely teaches a method for isolating DNA, RNA and proteins from the same sample (pg. 378, paragraph 2). Therefore the method steps are combinable. The combined teachings of magnetic solid supports comprising glass surface of Kleiber et al, magnetic beads comprising ion exchange resins of Lubenow et al provide the first and the second magnetic particulate solid supports for isolating nucleic acids and proteins from the same sample for isolating the nucleic acids and proteins from small amounts of the sample for genetic and protein analysis as taught by Schubler et al.

It would have been prima facie obvious to one having ordinary skill in the art at the time the claimed invention was made to include the nucleic acids and proteins isolation from the same sample of Schubler et al with the nucleic acids and proteins isolation method of Kleiber et al and Lubenow et al with a reasonable expectation of success.

An artisan would have been motivated to include the nucleic acids and protein isolation method from the same sample of Schubler et al with the expected benefit of using the small amounts of the sample for genetic and protein analysis as taught by Schubler et al (Figs. 1 and 2 and pg. 378, first paragraph and pg. 379, last paragraph). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves using the same sample for isolating nucleic acids and proteins from the same sample, which is also routinely practiced in the art as exemplified by Schubler et al.

Regarding claim 2, as described above while rejecting claim 1 Kleiber et al teaches that the biological sample comprises bacteria and cells isolated from human and animal cells that contain DNA and RNA components (column 5, lines 15-22) and further teaches magnetic particles with glass surface that bind to the nucleic acids (Fig. 1 and column 8, lines 8-56), which includes DNA and RNA.

Regarding claims 3, 24 and 25, as described above while rejecting claim 1 Kleiber et al, Lubenow et al and Schubler et al teaches sample containing RNA. Kleiber et al teaches magnetic particles with glass surface for isolating nucleic acids (i.e., the first magnetic particulate solid supports). Lubenow et al teaches the magnetic particles with ion exchange interactions resins (i.e., the second magnetic particulate solid supports). Both Lubenow et al and Schubler et al teach magnetic particles comprising oligodT (i.e., the third particulate solid supports). The solid supports for the nucleic acids, RNA and proteins isolation of Kleiber et al, Lubenow et al and Schubler et al are distinct because they contain distinct surfaces suitable specific for nucleic acid, RNA and protein interactions. Schubler et al teaches isolating RNA components using oligodT as capture probes (Fig. 1 and pg. 378, paragraph 2).

Regarding claim 4, as described above while rejecting claim 1 Kleiber et al teaches magnetic particles with glass surface for isolating nucleic acids, Schubler et al teaches magnetic particles containing oligodT for isolating RNA and the DNA from the same sample. One having ordinary skill in the art would recognize use the magnetic capture beads for isolating nucleic acids (i.e., the DNA and the RNA) and the RNA in separate steps.

Regarding claim 5, Schubler et al teaches isolating nucleic acids and protein components from the same sample (Figs. 1 and 2).

Regarding claim 6, Schubler et al teaches that the RNA is mRNA (Fig. 1a and pg. 378, column 2, and paragraph 2).

Regarding claim 7, Schubler et al teaches that the DNA is genomic (Fig. 1b, and pg. 378, column 2, and paragraph 3).

Regarding claim 8, Kleiber et al teaches that the method comprises isolating the total DNA (column 5, lines 5-22).

Regarding claim 9, Schubler et al teaches that the nucleic acid components are isolated from human or animal cells (column 5, lines 15-22).

Regarding claim 10, Schubler et al teaches that the total protein component is isolated (Fig. 2 and pg. 379, column 1, and paragraph 2).

Regarding claim 11, Kleiber et al teaches that the sample is a biological sample (column 5, lines 15-22).

Regarding claims 12, 13 and 14, Kleiber et al teaches pretreating the sample by contacting with the solid supports comprising the antibody to isolate and separate the cells expressing the cognate antigens on the cell surface (Fig. 1 and column 8, lines 8-30), which encompasses a preliminary treatment step to free the nucleic acid and/or protein components from structures or entities in which they may be contained. It is noted that “contacting the sample with the plurality of first and the second particulate solid supports” as recited in instant claim 13 is not active step because only subjecting the sample to cell isolation is the active method step.

Regarding claim 15, Kleiber et al teaches that the sample is subjected to cell lysis step prior to contacting with solid support (Fig. 1 and column 8, lines 33-35). It is noted that “contacting the sample with the first plurality of solid supports” as recited in claim 15 is not active step because only the cell lysis step is the active method step.

Regarding claim 16, Kleiber et al teaches subjecting the isolated cells from the sample to a magnetic field and washing steps to separate the isolated cells to remove contaminants along with the medium surrounding the cells (column 8, lines 13-33), which encompasses subjecting cells to an invitro modification procedure (i.e., removal of contaminants and medium) prior to the cell lysis step.

Regarding claim 17, Schubler et al teaches that the same cell lysate is used for nucleic acid and protein isolation thus teaching that the sample is not divided at any stage of the method (pgs. 378 and 379).

Regarding claim 18, Schubler et al teaches sample is divided (i.e., transferring) after grinding, i.e., preliminary treatment step (pg. 378, column 2, paragraph 2).

Regarding claim 19, Schubler et al teaches that the sample is processed sequentially (pgs. 378 and 379).

Regarding claim 20, Schubler et al teaches that RNA is isolated first, then DNA and then protein (pgs. 378 and 379), which meet the limitation of claim, because steps may be performed in any order.

Regarding claim 21, Kleiber et al teaches that the magnetic glass particle surface binding to the nucleic acid components comprises a hydroxyl group (i.e., Si-OH; column 3, lines 14-57).

Regarding claims 22 and 23, Kleiber et al teaches that the cells are lysed with the detergent and the magnetic glass particles are added to the lysis mixture for suitable period of time for the lysis to take place and binding of the nucleic acid components to the particle surface (Fig. 1 and column 8, lines 33-43), thus teaching cell lysis and nucleic acid binding to the plurality of magnetic particles occur concomitantly.

Regarding claim 34, Kleiber et al teaches that the magnetic particles comprises a glass surface with Si-OH group and (column 3, lines 40-57) and further teaches that the particles are in chaotropic saline solution (column 7, lines 40-52), which comprises water. The Si-OH groups on the glass surface in water acquire negative charges as evidenced by Behrens et al (pg. 6716, column 1, paragraph 2). The magnetic glass surface (i.e., the first particulate solid supports) comprising Si-OH groups in water of Kleiber et al have negative surface charges as further evidenced by Behrens et al.

11. Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kleiber et al (USPN 6,255,477 issued Jul. 3, 2001), Lubenow et al (USPN 6,723,510 issued Apr. 20, 2004) in view of Schubler et al (TIG, 1995, 11, 378-379) as applied to claims 1 and 15 as above and further in view of Petersen et al (USPGPUB 2001/0012612, published Aug. 9, 2001).

Claim 36 is dependent from claim 15. Claims 15 and 34 are dependent from claim 1. The teachings of Kleiber et al, Lubenow et al and Schubler et al regarding claims 1 and 15 are described above in section 10.

Regarding claim 35, Kleiber et al teaches contacting the sample with the plurality of magnetic particles comprising the glass surface (i.e., the first particulate solid supports) in the presence of a plurality of magnetic particles comprising the antibodies to bind cells (i.e., a plurality of solid particles; Fig. 1 and column 8, lines 9-56). Kleiber et al also teaches the magnetic particles of larger and smaller sizes (column 6, lines 40-50). Kleiber et al, Lubenow et al and Schubler et al do not teach that the first particulate solid supports and the plurality of solid particles are of different size.

Regarding claim 36, Kleiber et al teaches a plurality of magnetic particles comprising the antibodies (i.e., a plurality of solid particles) to isolate the cells and further teaches lysing the sample to release the nucleic acids (Fig. 1 and column 8, lines 9-56). ). Kleiber et al also teaches the magnetic particles of larger and smaller sizes (column 6, lines 40-50). Kleiber et al, Lubenow et al and Schubler et al do not teach that the first particulate solid supports and the plurality of solid particles are of different size.

However, solid supports having different sizes were known in the art at the time the claimed invention was made as taught by Petersen et al.

Petersen et al teaches a method for isolating the nucleic acids and proteins comprising first set of beads coated with antibodies for binding target cells and second set of beads for isolating nucleic acids (paragraph 0075). Petersen et al also teaches that the first set of beads is of different sizes than the second set of beads (paragraph 0072). Petersen et al also teaches having one size of beads to capture target cells and another size beads to capture nucleic acids from the said cell is useful for separating

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solid supports and for isolating nucleic acids and for subsequent elution and analysis (paragraph 0075).

It would have been prima facie obvious to one having ordinary skill in the art at the time the claimed invention was made to include the different size solid supports (i.e., the beads) of Petersen et al with the nucleic acid and protein isolation method of Kleiber et al, Lubenow et al and Schubler et al with a reasonable expectation of success.

An artisan would have been motivated to include the different size solid supports (i.e., the beads) of Petersen et al with the expected benefit of having one size of beads to capture target cells and another size beads to capture nucleic acids from the cells and for easy separation of solid supports and for isolating target nucleic acids and for subsequent elution and analysis as taught by Petersen et al (paragraph 0075). An artisan having ordinary skill in the art would have reasonable expectation of success because it merely involves substituting larger and smaller size particles of Kleiber et al with one size particle for isolating the cells and other size particle for capturing the nucleic acids for further analysis, which is also routinely practiced in the art as exemplified by Petersen et al.

### ***Response to Remarks from the Applicant***

#### ***Claim Rejections under 35 U.S.C. § 103(a)***

12. Applicant's arguments with respect to claims 1, 3, 5-12, 15-20, 24 and 25 rejected under 35 USC 103(a) as being unpatentable over Schubler et al in view of Lubenow et al have been fully considered (Remarks, pgs. 6-8, section A) and are

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persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new grounds of rejection are made in view of combination of references as described above in sections 10 and 11.

Applicant's arguments with respect to claims 1, 2 and 22 rejected under 35 USC 103(a) as being unpatentable over Schubler et al in view of Lubenow et al and further in view of Ekenberg et al have been fully considered (Remarks, pgs. 8-9, section B) and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new grounds of rejection are made in view of combination of references as described above in sections 10 and 11.

Applicant's arguments with respect to claims 1, 3-4, 13-14, 21 and 23 rejected under 35 USC 103(a) as being unpatentable over Schubler et al in view of Lubenow et al and further in view of Safarik et al have been fully considered (Remarks, pgs. 9-10, section C) and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new grounds of rejection are made in view of combination of references as described above in sections 10 and 11.

### ***Conclusion***

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Narayan K. Bhat/

Examiner, Art Unit 1634

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